PATENT
–EXPEDITED PROCESSING: REQUEST FOR RECONSIDERATION UNDER 37 CFR 1.116–

Docket No. 10806-155
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IN THE UNITED STATES PATENT & TRADEMARK OFFICE

Applicant:	Barbro Hemmendorff et al	:	Paper No.:	
Serial No.:	09/743,023	:	Group Art Unit:	1637
Filed:	March 7, 2001	:	Examiner:	Chunduru, Suryaprabha

For: **METHOD FOR THE PRODUCTION OF THE RECOMBINANT PEPTIDES WITH A LOW AMOUNT OF TRISULFIDES**

REQUEST FOR RECONSIDERATION UNDER 37 C.F.R. 1.116

Box AF
Commissioner for Patents
Washington, DC 20231

Dear Sir:

In response to the Official Action dated September 24, 2002, Applicants request reconsideration of the patentability of claims 1-3, 5-8 and 11-22, in view of the following remarks.

REMARKS

The Official Action dated September 24, 2002 has been carefully considered. Accordingly, the remarks presented herewith are believed sufficient to place the present application in condition for allowance. Reconsideration is respectfully requested.

Claim 20 was objected to as being a substantial duplicate of claim 2. This objection is traversed and reconsideration is respectfully requested. Particularly, the method of claim 2 is different from the method of claim 20. More particularly, claim 2 is directed to a method for the reduction of the amount of trisulfides in the production of recombinant peptides, while claim 20 is directed to a method for the reduction in the formation of the amount of trisulfides in the production of recombinant peptides. It is therefore submitted that method of claim 20 is not a substantial duplicate of the method of claim 2, and that the objection has been overcome. Reconsideration is respectfully requested.

Claims 1-3, 5-8, and 11-22 were rejected under 35 U.S.C. §102(e) as being anticipated by Builder et al, U.S. Patent No. 5,663,304. The Examiner asserted that Builder et al teach a method for production of recombinant peptides comprising fermenting cells to produce recombinant peptides in the presence of metal salt prior to peptide isolation. The Examiner also asserted that Builder et al teach the use of metals facilitates disulfide oxidation of polypeptides and yields correct refolding of a misfolded polypeptide contained in host cells. Finally, the Examiner asserted that the claimed methods are inherently disclosed by Builder et al as the reference discloses the use of a special buffer to avoid the possibility of producing polypeptides containing disulfide adducts which favor refolding of a misfolded polypeptide.

However, as will be set forth in detail below, Applicants submit that the methods defined by claims 1-3, 5-8 and 11-22 are not anticipated by Builder et al. Accordingly, this rejection is traversed, and reconsideration is respectfully requested.

The Examiner asserted that the limitation in the preamble of the claim is not given patentable weight. However, the Manual Patent Examining Procedure §2111.02 states that "the claim preamble must be read in the context of the entire claim. The determination of

whether preamble recitations are structural limitations or mere statements of purpose or use 'can be resolved only on review of the entirety of the [record] to gain an understanding of what the inventors actually invented and intended to encompass by the claims'. *Corning Glass Works v. Sumitomo Elec. U.S.A., Inc.*, 9 USPQ2d 1962, 1966 (Fed. Cir. 1989)". As disclosed in the specification and recited in the claims, the inventors have invented methods for the production of recombinant peptides with a low amount of trisulfides, methods for the reduction of the amount of trisulfides in the production of recombinant peptides, and a method for the reduction in the formation of the amount of trisulfides in the production of recombinant peptides. It is clear from the entirety of the record that the preamble recites a limitation of the present method claims and thus, should be given patentable weight.

Accordingly, claim 1 is directed to a method for the production of recombinant peptides with a low amount of trisulfides. The method comprises fermenting cells to produce the recombinant peptides. A metal salt is added during or after the fermentation step, prior to peptide isolation.

According to claim 2, the invention is directed to a method for the reduction of the amount of trisulfides in the production of recombinant peptides. The method comprises fermenting cells to produce recombinant peptides. A metal salt is added during or after fermentation, prior to peptide isolation.

According to claim 20, the invention is directed to a method for the reduction in the formation of the amount of trisulfides in the production of recombinant peptides. The method comprises fermenting cells to produce recombinant peptides. A metal salt is added during or after fermentation, prior to peptide isolation.

Builder et al disclose a method for increasing the yield of correct refolding of a misfolded polypeptide, specifically IGF-I, and reactivating misfolded IGF-I contained in host

cells. While Builder et al disclose that metal salts are provided in the fermentation medium, Applicants find no teaching, suggestion, or reference for reducing trisulfide formation in the production of recombinant peptides, as presently claimed. Builder et al only broadly assert that the medium may be "supplemented as necessary" with various components including, among others, salts (column 15, line 65--column 16, line 12). Applicants find no teaching, suggestion or reference for using a metal salt for reducing trisulfide formation in the production of recombinant peptides.

Moreover, the presently claimed methods are not inherent in the teachings of Builder et al. Builder et al teach the facilitation of disulfide oxidation of polypeptides, while the present invention teaches the reduction of trisulfide bond formation by the inhibition of H_2S activity. In addition, a disulfide adduct, as disclosed in Builder et al, is the product of the interaction between a protein and a reducing agent, such as glutathione, and thus, a disulfide adduct does not "inherently comprise" trisulfide bonds as the Examiner appears to assert. Further, as acknowledged by the Examiner, IGF-I is not known to produce trisulfides when the polypeptide is formed. Finally, Builder et al fail to provide a specific teaching in the Examples of the production of a peptide such as growth hormone which involves trisulfide formation. Thus, the methods presently claimed are not inherent in the teachings of Builder et al.

"Anticipation requires that every limitation of the claim in issue be disclosed, either expressly or under principles of inherency, in a single prior art reference." *Corning Glass Works v. Sumitomo Electric U.S.A. Inc., supra* at 1965, *citing Kalman v. Kimberly-Clark Corp.*, 218 USPQ 781, 789 (Fed. Cir. 1983), *cert. denied*, 224 USPQ 520 (1984). Inherency may not be established by "probabilities or possibilities." *Scaltech, Inc. v. Retec/Tetra, LLC.*, 51 USPQ2d 1055, 1059 (Fed. Cir. 1999). "The mere fact that a certain thing may result from

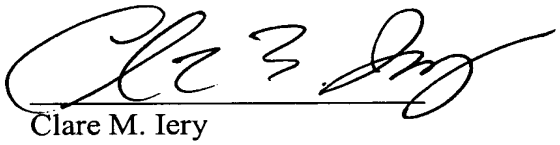
a given set of circumstances is not sufficient." *In re Oelrich*, 212 USPQ 323, 326 (CCPA 1981).

In view of the failure of Builder et al to disclose, either expressly or under principles of inherency, methods for the production of recombinant peptides with a low amount of trisulfides, methods for the reduction of the amount of trisulfides in the production of recombinant peptides, and a method for the reduction in the formation of the amount of trisulfides in the production of recombinant peptides, Builder et al do not disclose each element of the present claims, and therefore do not anticipate claims 1-3, 5-8 and 11-22 under 35 U.S.C. §102(e).

It is therefore submitted that the methods defined by present claims 1-3, 5-8 and 11-22 are not anticipated by Builder et al, and that the rejection under 35 U.S.C. §102(e) has been overcome. Reconsideration is respectfully requested.

It is believed that the above represents a complete response to the Examiner's objection and rejection under 35 U.S.C. §102, and places the present application in condition for allowance. Reconsideration and an early allowance are requested.

Respectfully submitted,



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